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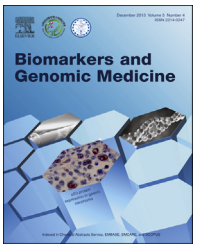

ORIGINAL ARTICLE

Microbiology of neonatal septicemia in a tertiary hospital in Benin City, Nigeria

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Abstract Septicemia is a major cause of death in neonates. Prompt diagnosis and effective treatment is necessary to treat patients with septicemia. However, the prevalence, etiology, and antibiotic susceptibility vary with location and time. This study aimed at determining the prevalence of neonatal septicemia and the effect of age and sex on this prevalence. In addition, the antibacterial susceptibility of etiologic agents was also determined. Blood samples were collected from 534 neonates (322 males and 212 females) between 1 day and 28 days of age with signs and symptoms of septicemia. The blood samples were processed to diagnose septicemia. Identification of bacterial isolates and disc susceptibility testing were performed using standard techniques. Age and sex did not significantly affect the prevalence of neonatal septicemia ($p = 0.554$ and 0.127, respectively). *Klebsiella* species were the predominant microorganism causing neonatal septicemia, in males and within the first 14 days of life. Fluoroquinolones, gentamicin, and β-lactams (with the exception of cloxacillin) were the most active antibacterial agents. An overall neonatal septicemia prevalence rate of 38.95% was observed. Klebsiella species was the most predominant isolate causing neonatal septicaemia. The β-lactam antibiotics recommended in susceptibility testing and the data collected in this study will be helpful in empiric therapy of neonatal septicemia.

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Introduction

Bloodstream infections cause significant morbidity and mortality among populations worldwide, and they are amongst the most common health-care-associated infections.[1]

Amongst them, neonatal sepsis is one of the most common reasons for admission to neonatal units in developing countries.[2] Septicemia in neonates refers to generalized bacterial infections with a positive blood culture in the first 4 weeks of life.[3] Neonatal blood culture-positive rates ranging from 25% to 55% have been reported in previous studies carried out in Nigeria.[4] Septicemia is a major cause of death in neonates and children.[5] Because neonatal septicemia is a life-threatening emergency, the knowledge of epidemiological and antimicrobial susceptibility pattern of common pathogens in a given area helps to inform the available choice of antibiotics. Predominance of either the Gram-positive or Gram-negative bacterial isolates is influenced by geographical location and changes in time, and therefore, the antibiotic susceptibility pattern is also influenced by location and time.[4] Thus, it is necessary to conduct periodic reviews. Against this background, this study aims at determining the prevalence of neonatal septicemia and the effect sex and age on this prevalence. The etiologic agents and their antibiotic susceptibility profiles were also determined.

Materials and methods

Study population

This study was carried out from February 1, 2010 to January 31, 2011 at the University of Benin Teaching Hospital, Benin City, Nigeria. Verbal informed consent was obtained from parents of neonates recruited in this study before the collection of blood samples. This study has been approved by the Ethical Committee of the University of Benin Teaching Hospital. A total of 534 neonates between 1 day and 28 days of age with clinical signs and symptoms of septicemia were recruited in this study. The signs and symptoms of septicemia were fever in neonates, fever in mother at the time of delivery, cloudy or smelly amniotic fluid, rapid pulse, rapid breathing, seizures, nausea, and vomiting. The study population consisted of 322 male and 212 female neonates.

Isolation of etiologic agents and antibacterial susceptibility testing

Blood samples were collected from each patient and dispensed into blood culture bottles (glucose broth and thioglycolate broth) and incubated for a maximum of 7 days. Bottles with signs of growth, such as turbidity, hemolysis, clot formation, gas production, and/or cotton ball effect were subcultured on chocolate, blood, and MacConkey agar plates. The chocolate agar plates were incubated in candle jar, while the blood agar and MacConkey agar plates were incubated aerobically. Significant bacterial isolates were identified by standard techniques.[6] Disc diffusion susceptibility testing was performed using the British Society for Antimicrobial Chemotherapy method.[7]

Statistical analysis

The data were analyzed with the Chi-square test using the statistical software INSTAT (GraphPad Software Inc., La Jolla, CA, USA).

Results

Effect of age and sex on the prevalence of neonatal septicemia

The effect of age and sex on the prevalence of neonatal septicemia is shown in Table 1. Although the prevalence of neonatal septicemia is higher in females than in males, the difference in prevalence between females and males was not statistically significant ($p = 0.127$). Similarly, there is no remarkable divergence in the prevalence of neonatal septicemia in different age groups ($p = 0.554$).

Distribution of etiologic agents of neonatal septicemia by sex

Among the etiologic agents isolated, *Klebsiella* species were the most predominant agent causing septicemia. *Staphylococcus aureus* was the second most prevalent isolate. *Klebsiella* species were more commonly found in males than in females. By contrast, *S. aureus* was more frequently isolated in females than in males (Table 2).

Distribution of etiologic agents of neonatal septicemia by age

In terms of age, *Klebsiella* species and *S. aureus* were the most prevalent microorganisms in the different age groups studied. *Klebsiella* species were the most prevalent organism in the 1—7- and 8—14-day-old neonates. *Klebsiella* species and *S. aureus* were the most prevalent isolates with a prevalence of 37.5% in the 15—21-day-old neonates. *S. aureus* was the most prevalent agent in the 22—28-day-old neonates, with a prevalence rate of 50% (Table 3).

Table 1 Effect of age and sex on the prevalence of neonatal septicemia.

	No. of neonates tested	No. of neonates infected (%)	*p*
Sex			0.127
Male	322	117 (36.34)	
Female	212	91 (42.92)	
Age (d)			0.554
1—7	457	174 (38.07)	
8—14	50	20 (40.00)	
15—21	15	8 (53.33)	
22—28	12	6 (50.00)	

d = days.

Table 2 Distribution of etiologic agents of neonatal septicemia by sex.

Organisms	No. of isolates (%) from males	No. of isolates (%) from female	Total no. of isolates (%)
Escherichia coli	6 (5.13)	4 (4.39)	10 (4.80)
Klebsiella species	45 (38.46)	29 (31.87)	74 (35.57)
Enterobacter species	3 (2.56)	2 (2.19)	5 (2.40)
Citrobacter species	3 (2.56)	2 (2.19)	5 (2.40)
Proteus vulgaris	2 (1.71)	3 (3.29)	5 (2.40)
Proteus mirabilis	3 (3.56)	5 (5.49)	8 (3.84)
Providencia species	4 (3.42)	2 (2.19)	6 (2.88)
Acinetobacter species	5 (4.27)	4 (4.39)	9 (4.32)
Alcaligenes species	9 (7.69)	3 (3.29)	12 (5.76)
Pseudomonas aeruginosa	3 (3.56)	5 (5.49)	8 (3.84)
Staphylococcus aureus	34 (29.05)	32 (35.16)	66 (31.73)
Total	117 (56.25)	91 (43.75)	208

Numbers in parentheses are percentages.

Antibacterial susceptibility profile

The susceptibility profile of bacterial agents of neonatal septicemia is shown in Table 4. Fluoroquinolones exhibited very high activity against all isolates tested. The β-lactams showed moderate to high activity, with the exception of cloxacillin, which showed no activity against *S. aureus* isolates. Gentamicin had activity similar to that of β-lactams. Erythromycin, chloramphenicol, tetracycline, and sulfamethoxazole—trimethoprim showed no activity against the bacterial isolates.

Discussion

Septicemia is a major cause of death in neonates and children.[5] Bacterial agents of septicemia and their susceptibility to antibiotics are influenced by geographical location and time,[4] thus necessitating periodic reviews of bacterial septicemia to aid in empiric therapy of this life-threatening condition. This study focused on determining the prevalence of neonatal septicemia among neonates as well as identifying the etiologic agents and their susceptibility profiles. An overall neonatal septicemia prevalence rate of 38.95% was observed in this study. This result is higher than that of the value previously reported.[4,8] However, it is lower than the 55% that has been documented in previous studies in Nigeria.[9] These reports further confirm that the prevalence of septicemia varies from one location to another, as well as with time, even within the same location.

The finding of this study that sex and age did not affect the prevalence of septicemia agrees with a previous report.[10] However, that study was not restricted to neonates.[10] Among neonates, it has been reported that male sex is a risk factor for septicemia.[11] This observation is not in agreement with the findings in this study. Differences in geographical location and time of the study may explain the variation in the findings as these two factors have been reported to affect the prevalence of septicemia.[4] The finding that *Klebsiella* species was the most prevalence isolate overall agrees with previous reports.[8,12,13] However,

Table 3 Distribution of etiologic agents of neonatal septicemia by age.

Organisms	Age (d)			
	1—7	8—14	15—21	22—28
Escherichia coli	9 (5.17)	0	0	1 (16.67)
Klebsiella species	59 (33.90)	10 (50.00)	3 (37.50)	2 (33.33)
Enterobacter species	3 (4.29)	1 (5.00)	0	0
Citrobacter species	5 (2.87)	0	0	0
Proteus vulgaris	5 (2.87)	0	0	0
Proteus mirabilis	8 (4.59)	0	0	0
Providencia species	6 (3.44)	0	0	0
Acinetobacter species	6 (3.44)	2 (10.00)	1 (12.50)	0
Alcaligenes species	10 (5.74)	1 (5.00)	1 (12.50)	
Pseudomonas aeruginosa	8 (4.59)	0	0	0
Staphylococcus aureus	54 (31.03)	6 (30.00)	3 (37.50)	3 (50.00)
Total	174 (83.65)	20 (9.62)	8 (3.85)	6 (2.88)

Figures in parentheses are percentages.
d = day.

Table 4 Susceptibility profile of bacterial agents of neonatal septicemia.

Organisms	Antibacterial agents (μg/disc)										
	OFX (5)	CIP (5)	CN (10)	AUG (10)	SXT (25)	OB (5)	TE (10)	CXM (30)	C (10)	E (5)	CRO (30)	CAZ (30)
Escherichia coli ($N = 10$)	10 (100.0)	10 (100.0)	6 (60.0)	10 (100.0)	0 (0.0)	ND	0 (0.0)	8 (80.0)	0 (0.0)	ND	9 (90.0)	8 (80.0)
Klebsiella spp. ($N = 74$)	74 (100.0)	74 (100.0)	69 (93.2)	71 (95.9)	0 (0.0)	ND	0 (0.0)	71 (95.9)	0 (0.0)	ND	70 (94.6)	70 (94.6)
Enterobacter spp. ($N = 5$)	5 (100.0)	5 (100.0)	0 (0.0)	3 (60.0)	0 (0.0)	ND	0 (0.0)	3 (60.0)	0 (0.0)	ND	5 (100.0)	4 (80.0)
Citrobacter freundii ($N = 5$)	5 (100.0)	5 (100.0)	3 (60.0)	5 (100.0)	0 (0.0)	ND	0 (0.0)	3 (60.0)	0 (0.0)	ND	4 (80.0)	2 (40.0)
Proteus vulgaris ($N = 5$)	5 (100.0)	5 (100.0)	5 (100.0)	5 (100.0)	0 (0.0)	ND	0 (0.0)	4 (80.0)	0 (0.0)	ND	4 (80.0)	4 (80.0)
Proteus mirabilis ($N = 8$)	8 (100.0)	8 (100.0)	4 (50.0)	8 (100.0)	0 (0.0)	ND	0 (0.0)	4 (50.0)	0 (0.0)	ND	6 (75.0)	7 (87.5)
Providencia spp. ($N = 6$)	6 (100.0)	6 (100.0)	3 (50.0)	6 (100.0)	0 (0.0)	ND	0 (0.0)	4 (66.7)	0 (0.0)	ND	5 (83.3)	4 (66.71)
Acinetobacter spp. ($N = 9$)	9 (100.0)	9 (100.0)	4 (44.4)	9 (100.0)	0 (0.0)	ND	0 (0.0)	5 (55.6)	0 (0.0)	ND	6 (66.7)	6 (66.7)
Pseudomonas aeruginosa ($N = 8$)	8 (100.0)	6 (75.6)	4 (50.0)	4 (50.0)	0 (0.0)	ND	0 (0.0)	0 (0.0)	0 (0.0)	ND	4 (50.0)	3 (37.5)
Alcaligenes spp. ($N = 12$)	10 (83.3)	9 (75.5)	6 (50.0)	8 (66.7)	0 (0.0)	ND	0 (0.0)	6 (50.0)	0 (0.0)	ND	7 (58.3)	7 (58.3)
Staphylococcus aureus ($N = 66$)	66 (100.0)	63 (95.5)	60 (90.9)	63 (95.5)	0 (0.0)	0 (0.0)	0 (0.0)	64 (96.9)	0 (0.0)	0 (0.0)	63 (95.5)	61 (92.4)

Data are expressed in number of susceptible isolates (percentage susceptibility).
AUG = cloxacillin/clavulanic acid; C = chloramphenicol; CN = gentamicin; CAZ = ceftriaxone; CIP = ciprofloxacin; CRO = ceftazidime; CXM = cefuroxime; E = erythromycin; ND = not done; OB = cloxacillin; OFX = ofloxacin; SXT = sulfamethoxazole–trimethoprim; TE = tetracycline.

it disagrees with other studies in which *S. aureus* predominated in neonate septicemia.[3,4,11] With regard to sex, *Klebsiella* species was predominantly found in males (38.5%), whereas *S. aureus* was predominantly found in females (35.16%). All isolates recovered in this study appeared as causative agents of early-onset septicemia (within the first 7 days), with *Klebsiella* species predominating. Some authors did not report *Klebsiella* species as the cause of early-onset septicemia in their study.[11,14] However, Vergnano et al[13] reported *Klebsiella* species to be associated with both early-onset septicemia and late-onset septicemia. Their report agrees with the findings of our study. This study revealed that *Klebsiella* species were still the most prevalent agent of septicemia in neonates aged less than 8 and 14 days, whereas in 15- and 21-day-old neonates, both *Klebsiella* species and *S. aureus* predominate as agents of septicemia with a prevalence of 37.5% each. However, in 22–28-day-old neonates, *S. aureus* predominated. This may indicate a changing pattern in the etiology of neonatal septicemia as the age increases.

Antibiotic resistance is a global problem and reports of multiresistant bacteria causing neonatal sepsis in developing countries are increasing.[14] Spread of resistant organisms in hospital is a recognized problem and babies admitted from the community may also carry resistant pathogens.[15] The wide availability of over-the-counter sale of antibiotics without prescriptions and the inappropriate use of broad-spectrum antibiotics in the community have been suggested as possible reasons for increasing resistance among community isolates.[12,16] Erythromycin, chloramphenicol, cloxacillin, tetracycline, and sulfamethoxazole–trimethoprim were not active against any bacterial isolates. This may be due to their long-term usage and low cost. Fluoroquinolones, gentamicin, and β-lactam (with the exception of cloxacillin) showed moderate to very good activity against the bacterial isolates. The fluoroquinolones are contraindicated in children.[17] Therefore, β-lactam and gentamicin would be most appropriate in the management of septicemia in our institution. However, gentamicin has toxic side effects in patients with renal impairment.[17] This is important because urinary tract infection is the main reason for prolonged jaundice in neonates.[18] Jaundice is one of the most common problems during the neonatal period.[19] Therefore, gentamicin maybe contraindicated. Amoxicillin–clavulanate and the cephalosporins appear to be the drug of choice in managing neonatal septicemia depending on the bacteria isolates.

An overall neonatal septicemia prevalence rate of 38.95% was observed in this study. *Klebsiella* species were the most predominant isolates causing early-onset septicemia in neonates. β-Lactam, fluoroquinolones, and gentamicin were the most active antibacterial agents. The data presented here will be helpful in the empiric management of neonatal septicemia.

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